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<110> Human Genome Sciences, Inc.

<120> Albumin Fusion Proteins

<130> PF544PCT

<140> Unassigned

<141> 2001-04-12

<150> 60/229,358

<151> 2000-04-12

<150> 60/256,931

<151> 2000-12-21

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<151> 2000-04-25

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<170> PatentIn Ver. 2.1

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gaa aat ttc aaa gcc ttg gtg ttg att gcc ttt gct cag tat ctt cag 96
 Glu Asn Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln
 20 25 30

cag tgt cca ttt gaa gat cat gta aaa tta gtg aat gaa gta act gaa 144
 Gln Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu
 35 40 45

ttt gca aaa aca tgt gtt gct gat gag tca gct gaa aat tgt gac aaa 192
 Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys
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tca ctt cat acc ctt ttt gga gac aaa tta tgc aca gtt gca act ctt 240
 Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu
 65 70 75 80

cgt gaa acc tat ggt gaa atg gct gac tgc tgt gca aaa caa gaa cct 288
 Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro
 85 90 95

gag aga aat gaa tgc ttc ttg caa cac aaa gat gac aac cca aac ctc 336
 Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu
 100 105 110

ccc cga ttg gtg aga cca gag gtt gat gtg atg tgc act gct ttt cat 384
 Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His
 115 120 125

gac aat gaa gag aca ttt ttg aaa aaa tac tta tat gaa att gcc aga 432
 Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg
 130 135 140

aga cat cct tac ttt tat gcc ccg gaa ctc ctt ttc ttt gct aaa agg 480

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Tyr	Lys	Ala	Ala	Phe	Thr	Glu	Cys	Cys	Gln	Ala	Ala	Asp	Lys	Ala	Ala	
				165					170					175		
tgc	ctg	ttg	cca	aag	ctc	gat	gaa	ctt	cgg	gat	gaa	ggg	aag	gct	tcg	576
Cys	Leu	Leu	Pro	Lys	Leu	Asp	Glu	Leu	Arg	Asp	Glu	Gly	Lys	Ala	Ser	
			180					185					190			
tct	gcc	aaa	cag	aga	ctc	aaa	tgt	gcc	agt	ctc	caa	aaa	ttt	gga	gaa	624
Ser	Ala	Lys	Gln	Arg	Leu	Lys	Cys	Ala	Ser	Leu	Gln	Lys	Phe	Gly	Glu	
		195					200					205				
aga	gct	ttc	aaa	gca	tgg	gca	gtg	gct	cgc	ctg	agc	cag	aga	ttt	ccc	672
Arg	Ala	Phe	Lys	Ala	Trp	Ala	Val	Ala	Arg	Leu	Ser	Gln	Arg	Phe	Pro	
	210					215					220					
aaa	gct	gag	ttt	gca	gaa	gtt	tcc	aag	tta	gtg	aca	gat	ctt	acc	aaa	720
Lys	Ala	Glu	Phe	Ala	Glu	Val	Ser	Lys	Leu	Val	Thr	Asp	Leu	Thr	Lys	
225					230					235					240	
gtc	cac	acg	gaa	tgc	tgc	cat	gga	gat	ctg	ctt	gaa	tgt	gct	gat	gac	768
Val	His	Thr	Glu	Cys	Cys	His	Gly	Asp	Leu	Leu	Glu	Cys	Ala	Asp	Asp	
				245					250					255		
agg	gcg	gac	ctt	gcc	aag	tat	atc	tgt	gaa	aat	cag	gat	tcg	atc	tcc	816
Arg	Ala	Asp	Leu	Ala	Lys	Tyr	Ile	Cys	Glu	Asn	Gln	Asp	Ser	Ile	Ser	
			260					265					270			
agt	aaa	ctg	aag	gaa	tgc	tgt	gaa	aaa	cct	ctg	ttg	gaa	aaa	tcc	cac	864
Ser	Lys	Leu	Lys	Glu	Cys	Cys	Glu	Lys	Pro	Leu	Leu	Glu	Lys	Ser	His	
		275					280					285				
tgc	att	gcc	gaa	gtg	gaa	aat	gat	gag	atg	cct	gct	gac	ttg	cct	tca	912
Cys	Ile	Ala	Glu	Val	Glu	Asn	Asp	Glu	Met	Pro	Ala	Asp	Leu	Pro	Ser	
	290					295					300					
tta	gct	gct	gat	ttt	gtt	gaa	agt	aag	gat	gtt	tgc	aaa	aac	tat	gct	960
Leu	Ala	Ala	Asp	Phe	Val	Glu	Ser	Lys	Asp	Val	Cys	Lys	Asn	Tyr	Ala	
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gag	gca	aag	gat	gtc	ttc	ctg	ggc	atg	ttt	ttg	tat	gaa	tat	gca	aga	1008
Glu	Ala	Lys	Asp	Val	Phe	Leu	Gly	Met	Phe	Leu	Tyr	Glu	Tyr	Ala	Arg	
				325					330					335		
agg	cat	cct	gat	tac	tct	gtc	gtg	ctg	ctg	ctg	aga	ctt	gcc	aag	aca	1056
Arg	His	Pro	Asp	Tyr	Ser	Val	Val	Leu	Leu	Leu	Arg	Leu	Ala	Lys	Thr	
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tat gaa acc act cta gag aag tgc tgt gcc gct gca gat cct cat gaa	1104
Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu	
355 360 365	
tgc tat gcc aaa gtg ttc gat gaa ttt aaa cct ctt gtg gaa gag cct	1152
Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro	
370 375 380	
cag aat tta atc aaa caa aac tgt gag ctt ttt gag cag ctt gga gag	1200
Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu	
385 390 395 400	
tac aaa ttc cag aat gcg cta tta gtt cgt tac acc aag aaa gta ccc	1248
Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro	
405 410 415	
caa gtg tca act cca act ctt gta gag gtc tca aga aac cta gga aaa	1296
Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys	
420 425 430	
gtg ggc agc aaa tgt tgt aaa cat cct gaa gca aaa aga atg ccc tgt	1344
Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys	
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gca gaa gac tat cta tcc gtg gtc ctg aac cag tta tgt gtg ttg cat	1392
Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His	
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gag aaa acg cca gta agt gac aga gtc aca aaa tgc tgc aca gag tcc	1440
Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser	
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ttg gtg aac agg cga cca tgc ttt tca gct ctg gaa gtc gat gaa aca	1488
Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr	
485 490 495	
tac gtt ccc aaa gag ttt aat gct gaa aca ttc acc ttc cat gca gat	1536
Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp	
500 505 510	
ata tgc aca ctt tct gag aag gag aga caa atc aag aaa caa act gca	1584
Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala	
515 520 525	
ctt gtt gag ctt gtg aaa cac aag ccc aag gca aca aaa gag caa ctg	1632
Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu	
530 535 540	
aaa gct gtt atg gat gat ttc gca gct ttt gta gag aag tgc tgc aag	1680
Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys	
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 35 40 45
 Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys
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 Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu
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 Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro
 85 90 95
 Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu
 100 105 110
 Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His
 115 120 125
 Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg
 130 135 140
 Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg
 145 150 155 160
 Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala
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 Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser
 180 185 190

Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu
 195 200 205
 Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro
 210 215 220
 Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys
 225 230 235 240
 Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp
 245 250 255
 Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser
 260 265 270
 Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His
 275 280 285
 Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser
 290 295 300
 Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala
 305 310 315 320
 Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg
 325 330 335
 Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr
 340 345 350
 Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu
 355 360 365
 Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro
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 Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu
 385 390 395 400
 Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro
 405 410 415
 Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys
 420 425 430
 Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys
 435 440 445
 Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His
 450 455 460

Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser
 465 470 475 480
 Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr
 485 490 495
 Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp
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 Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala
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the Therapeutic Protein

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<221> misc feature

<222> (44)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (45)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (46)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (47)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (48)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (49)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (50)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (51)

<223> n equals a,t,g, or c

<220>
 <221> misc feature
 <222> (52)
 <223> n equals a,t,g, or c

 <400> 28
 ctttaaactcg atgagcaacc tcactcttgt gtgcacnnnn nnnnnnnnnn nn 52

 <210> 29
 <211> 24
 <212> PRT
 <213> Artificial Sequence

 <220>
 <221> signal
 <223> signal peptide of natural human serum albumin protein

 <400> 29
 Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
 1 5 10 15
 Tyr Ser Arg Ser Leu Asp Lys Arg
 20

 <210> 30
 <211> 114
 <212> DNA
 <213> Artificial Sequence

 <220>
 <221> primer_bind
 <223> forward primer useful for generation of PC4:HSA
 albumin fusion VECTOR

 <220>
 <221> misc_feature
 <222> (5)..(10)
 <223> BamHI restriction site

 <220>
 <221> misc_feature
 <222> (11)..(16)
 <223> Hind III restriction site

 <220>
 <221> misc_feature
 <222> (17)..(27)
 <223> Kozak sequence

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<220>
<221> misc_feature
<222> (25)..(97)
<223> cds natural signal sequence of human serum albumin

<220>
<221> misc_feature
<222> (75)..(81)
<223> XhoI restriction site

<220>
<221> misc_feature
<222> (98)..(114)
<223> cds first six amino acids of human serum albumin

<400> 30
tcagggatcc aagcttccgc caccatgaag tgggtaacct ttatttcctt tctttttctc 60

tttagctcgg cttactcgag ggggtgtgtt cgtcgagatg cacacaagag tgag      114

<210> 31
<211> 43
<212> DNA
<213> Artificial Sequence

<220>
<221> primer_bind
<223> reverse primer useful for generation of
PC4:HSA albumin fusion VECTOR

<220>
<221> misc_feature
<222> (6)..(11)
<223> Asp718 restriction site

<220>
<221> misc_feature
<222> (12)..(17)
<223> EcoRI restriction site

<220>
<221> misc_feature
<222> (15)..(17)
<223> reverse complement of stop codon

<220>
<221> misc_feature
<222> (18)..(25)
<223> AscI restriction site

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<220>
 <221> misc_feature
 <222> (18)..(43)
 <223> reverse complement of DNA sequence encoding last 9 amino acids

 <400> 31
 gcagcgggtac cgaattcggc ggcgcttata agcctaaggc agc 43

 <210> 32
 <211> 46
 <212> DNA
 <213> Artificial Sequence

 <220>
 <221> primer_bind
 <223> forward primer useful for inserting Therapeutic
 protein into pC4:HSA vector

 <220>
 <221> misc feature
 <222> (29)
 <223> n equals a,t,g, or c

 <220>
 <221> misc feature
 <222> (30)
 <223> n equals a,t,g, or c

 <220>
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 <222> (31)
 <223> n equals a,t,g, or c

 <220>
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 <222> (32)
 <223> n equals a,t,g, or c

 <220>
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 <222> (33)
 <223> n equals a,t,g, or c

 <220>
 <221> misc feature
 <222> (34)
 <223> n equals a,t,g, or c

 <220>
 <221> misc feature
 <222> (35)

<223> n equals a,t,g, or c

<220>
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<222> (36)
<223> n equals a,t,g, or c

<220>
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<222> (37)
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<220>
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<222> (38)
<223> n equals a,t,g, or c

<220>
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<222> (39)
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<222> (41)
<223> n equals a,t,g, or c

<220>
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<222> (42)
<223> n equals a,t,g, or c

<220>
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<222> (43)
<223> n equals a,t,g, or c

<220>
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<222> (44)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (45)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (46)
<223> n equals a,t,g, or c

<400> 32
ccgccgctcg aggggtgtgt ttcgtcgann nnnnnnnnnn nnnnnn

46

<210> 33
<211> 55
<212> DNA
<213> Artificial Sequence

<220>
<221> primer_bind
<223> reverse primer useful for inserting Therapeutic
protein into pC4:HSA vector

<220>
<221> misc feature
<222> (38)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (39)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (40)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (41)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (42)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (43)
<223> n equals a,t,g, or c

<220>
<221> misc feature

<222> (44)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (45)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (46)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (47)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (48)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (49)
<223> n equals a,t,g, or c

<220>
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<222> (50)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (51)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (52)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (53)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (54)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (55)

<223> n equals a,t,g, or c

<400> 33

agtcccatcg atgagcaacc tcactcttgt gtgcatcnnn nnnnnnnnnn nnnnn 55

<210> 34

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<221> signal

<223> Stanniocalcin signal peptide

<400> 34

Met	Leu	Gln	Asn	Ser	Ala	Val	Leu	Leu	Leu	Leu	Val	Ile	Ser	Ala	Ser
1				5					10					15	

Ala

<210> 35

<211> 22

<212> PRT

<213> Artificial Sequence

<220>

<221> signal

<223> Synthetic signal peptide

<400> 35

Met	Pro	Thr	Trp	Ala	Trp	Trp	Leu	Phe	Leu	Val	Leu	Leu	Leu	Ala	Leu
1				5				10						15	

Trp	Ala	Pro	Ala	Arg	Gly
				20	

<210> 36

<211> 733

<212> DNA

<213> Homo sapiens

<400> 36

gggatccgga gcccaaattct tctgacaaaa ctacacatg cccaccgtgc ccagcacctg 60

aattcgaggg tgcaccgtca gtcttcctct tcccccaaaa acccaaggac accctcatga 120

tctcccgac tcctgaggtc acatgcgtagg tggtaggacgt aagccacgaa gaccctgagg	180
tcaagttcaa ctggtacgtg gacggcgtagg aggtgcataa tgccaagaca aagccgcggg	240
aggagcagta caacagcacg taccgtgtgg tcagcgtcct caccgtcctg caccaggact	300
ggctgaatgg caaggagtac aagtgcaagg tctccaacaa agccctccca acccccatcg	360
agaaaacccat ctccaaagcc aaagggcagc cccgagaacc acaggtgtac accctgcccc	420
catcccgga tgagctgacc aagaaccagg tcagcctgac ctgcctgggtc aaaggcttct	480
atccaagcga catcgccgtg gaggtaggaga gcaatgggca gccggagaac aactacaaga	540
ccacgcctcc cgtgctggac tccgacggct ccttcttctc ctacagcaag ctcaccgtgg	600
acaagagcag gtggcagcag gggaacgtct tctcatgctc cgtgatgcat gaggctctgc	660
acaaccacta cacgcagaag agcctctccc tgtctccggg taaatgagtg cgacggccgc	720
gactctagag gat	733

<210> 37
 <211> 5
 <212> PRT
 <213> Artificial sequence

<220>
 <221> misc_structure
 <223> membrane proximal motif of class 1 cytokine receptors

<220>
 <221> misc_feature
 <222> (3)
 <223> Xaa equals any

<400> 37
 Trp Ser Xaa Trp Ser
 1 5

<210> 38
 <211> 86
 <212> DNA
 <213> Artificial Sequence

<220>
 <221> primer_bind
 <223> forward primer useful for generation of a synthetic gamma
 activation site (GAS) containing promoter element

<400> 38
 gcgcctcgag atttccccga aatctagatt tccccgaaat gatttccccg aaatgatttc 60
 cccgaaatat ctgccatctc aattag 86

<210> 39
 <211> 27
 <212> DNA
 <213> Artificial Sequence

<220>
 <221> primer_bind
 <223> reverse primer useful for generation of a synthetic gamma
 activation site (GAS) containing promoter element

<400> 39
 gcggcaagct ttttgcaaag cctaggg 27

<210> 40
 <211> 271
 <212> DNA
 <213> Artificial Sequence

<220>
 <221> misc_feature
 <223> Synthetic GAS-SV40 promoter sequence

<400> 40
 ctcgagattt ccccgaatc tagatttccc cgaaatgatt tccccgaaat gatttccccg 60
 aaatatctgc catctcaatt agtcagcaac catagtcccg cccctaactc cgcccatccc 120
 gccctaact ccgcccagtt ccgcccattc tccgcccacat ggctgactaa ttttttttat 180
 ttatgcagag gccgaggccg cctcggcctc tgagctattc cagaagtagt gaggaggctt 240
 ttttgagggc ctaggctttt gcaaaaagct t 271

<210> 41
 <211> 32
 <212> DNA
 <213> Artificial Sequence

<220>
 <221> primer_bind
 <223> primer useful for generation of a EGR/SEAP reporter construct

<400> 41
 gcgctcgagg gatgacagcg atagaacccc gg 32

<210> 42
 <211> 31
 <212> DNA
 <213> Artificial Sequence

 <220>
 <221> primer_bind
 <223> primer useful for generation of a EGR/SEAP reporter construct

 <400> 42
 gcgaagcttc gcgactcccc ggatccgcct c 31

 <210> 43
 <211> 12
 <212> DNA
 <213> Artificial Sequence

 <220>
 <221> misc_binding
 <223> NF-KB binding site

 <400> 43
 ggggactttc cc 12

 <210> 44
 <211> 73
 <212> DNA
 <213> Artificial Sequence

 <220>
 <221> primer_bind
 <223> forward primer useful for generation of a vector containing the
 NF-KB promoter element

 <400> 44
 gcggcctcga ggggactttc ccggggactt tccggggact ttccgggact ttccatcctg 60

 ccatctcaat tag 73

 <210> 45
 <211> 256
 <212> DNA
 <213> Artificial Sequence

 <220>
 <221> misc_feature
 <223> Synthetic NF-KB/SV40 promoter

 <400> 45
 ctcgagggga ctttcccggg gactttccgg ggactttccg ggactttcca tctgccatct 60

caattagtca gcaaccatag tcccgccct aactccgcc atcccgcccc taactccgcc	120
cagttccgcc cattctccgc cccatggctg actaattttt tttatttatg cagaggccga	180
ggccgcctcg gcctctgagc tattccagaa gtagtgagga ggcttttttg gaggcctagg	240
cttttgcaaa aagctt	256